09/765,764
part of Dialog search

```
Set     Items   Description
S1        125   THYMIDYLATE(20N)(POLYMORPH? OR REPEAT)
S2         46   RD (unique items)
S3         28   S2 NOT PY>=1999
S4          2   S2(20N)(DRUG OR THERAP?)
S5       1959   THYMIDYLATE(20N)EXPRESSION
S6       2176   THYMIDYLATE(20N)EXPRESS?
S7        528   S6(20N)(CANCER OR TUMOR)
S8         68   S7(20N)(DRUG OR THERAP?)
S9         44   RD (unique items)
S10        28   S9 NOT PY>=1999
? s s10 not s3

             28  S10
             28  S3
     S11     27  S10 NOT S3
? t 11/5/all


 11/5/1     (Item 1 from file: 34)
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2001 Inst for Sci Info. All rts. reserv.

07002680   Genuine Article#: 113TM   Number of References: 15
Title: Thymidylate synthase as a predictor of response
Author(s): Leichman CG  (REPRINT)
Corporate Source: ROSWELL PK CANC INST,DIV MED, ELM & CARLTON
    ST/BUFFALO//NY/14263 (REPRINT)
Journal: ONCOLOGY-NEW YORK, 1998, V12, N8,6 (AUG), P43-47
ISSN: 0890-9091   Publication date: 19980800
Publisher: P R R INC, 17 PROSPECT ST, HUNTINGTON, NY 11743
Language: English   Document Type: ARTICLE
Geographic Location: USA
Subfile: CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: ONCOLOGY
Abstract: It has been hypothesized that intratumoral %thymidylate% synthase
    (TS) gene %expression% might be used to select %therapy% for patients
    with disseminated colorectal %cancer%. We recently reported the results
    of a clinical trial in 46 patients with disseminated or recurrent
    colorectal cancer testing whether expression of TS within the primary
    tumor, as assessed by quantitative polymerase chain reaction (PCR)
    methodology, would predict the responsiveness of that cancer to
    fluoropyrimidine-based therapy. This trial demonstrated that
    intratumoral TS/beta-actin messenger RNA (mRNA) ratio can accurately
    predict which metastatic colorectal tumors wilt be resistant to a
    leucovorin-modulated 5-FU infusion and which have a high likelihood of
    responding to such a regimen. Results of other studies of adjuvant
    therapy in gastric cancer and colorectal cancer also indicated that TS
    expression within the tumor is predictive of response to 5-FU-based
    therapy. It may be possible to use this parameter prospectively to
    decide which patients should receive fluorinated pyrimidine therapy:
    Patients whose tumors express low TS levels would be likely to benefit
    from such therapy, whereas limited preliminary data suggest that
    patients whose tumors express high TS levels may benefit from
    irinotecan (CPT-11 [Camptosar]).
 Identifiers--KeyWord Plus(R): DISSEMINATED COLORECTAL-CANCER;
    PROTRACTED-INFUSION; WEEKLY LEUCOVORIN; EXPRESSION; QUANTITATION;
    FLUOROURACIL
 Cited References:
```

BENSON AB, 1997, V16, P917, P AM SOC CLIN ONCOL
GREEN S, 1992, V10, P239, INVEST NEW DRUG
HORIKOSHI T, 1992, V52, P108, CANCER RES
IZZO J, 1992, V3, P1298, P AM ASS CAH RES
JOHNSTON PG, 1994, V12, P2640, J CLIN ONCOL
LEICHMAN CG, 1990, V26, P57, CANCER CHEMOTH PHARM
LEICHMAN CG, 1997, V15, P3223, J CLIN ONCOL
LEICHMAN CG, 1993, V85, P41, J NATL CANCER I
LEICHMAN L, 1995, V31, P1306, EUR J CANCER
LENZ HJ, 1996, V14, P176, J CLIN ONCOL
LENZ HJ, 1996, V15, P504, P AM SOC CLIN ONCOL
LENZ HJ, 1995, V4, P305, PCR METH APPL
LENZ HJ, 1994, REVERSE TRANSCRIPTAS
SALTZ L, 1998, V17, P1080, P AM SOC CLIN ONCOL
XIONG YP, 1997, V16, P918, P AM SOC CLIN ONCOL

11/5/2 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06705273 Genuine Article#: ZL982 Number of References: 49
Title: Restoration of wild-type p53 activity in p53-null HL-60 cells confers multidrug sensitivity
Author(s): Ju JF; Banerjee D; Lenz HJ; Danenberg KD; Schmittgen TC; Spears CP; Schonthal AH; Manno DJ; Hochhauser D; Bertino JR; Danenberg PV (REPRINT)
Corporate Source: UNIV SO CALIF,SCH MED, NORRIS COMPREHENS CANC CTR, 1303 N MISSION RD/LOS ANGELES//CA/90033 (REPRINT); UNIV SO CALIF,SCH MED, NORRIS COMPREHENS CANC CTR/LOS ANGELES//CA/90033; MEM SLOAN KETTERING CANC CTR,/NEW YORK//NY/10021
Journal: CLINICAL CANCER RESEARCH, 1998, V4, N5 (MAY), P1315-1322
ISSN: 1078-0432 Publication date: 19980500
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: ONCOLOGY
Abstract: HL-60 cells that stably express transfected wild-type (wt) p53 were used to determine whether restoration of wt p53 increased the chemosensitivity of cells that normally lack p53 activity. The wt p53 HL-60 transfectants (SN3 cells) were more sensitive than the parental (S) cells to a number of common anticancer drugs representing various mechanisms of action, whereas HL-60 cells transfected with p53 genes mutated at codons 248 and 143 were not sensitized. The sensitization ratio due to the transfected wt p53 varied from about 2-fold for cisplatin to over 50-fold for thymidine. Cells treated with the thymidylate synthase inhibitor 5-fluoro-2'-deoxyuridine (FdUrd) were used to study changes in various p53-associated gene expressions, A higher percentage of apoptotic cells among the SN3 cells was observed than among the S cells at each concentration of FdUrd, The S cells had undetectable levels of bar and high levels of bcl-2, whereas the SN3 cells had undetectable levels of bcl-2 levels and appreciable basal levels of bar. After FdUrd treatment of SN3 cells, both p53 and bar levels increased, but the induction of bar was faster than that of p53 and paralleled the appearance of apoptotic DNA laddering. FdUrd treatment induced p21 expression and increased the G(1) fraction of the SN3 cells but did not induce p21 or change the phase distribution in the S cells, FdUrd treatment also induced the expression and phosphorylation of cyclin D1 in the SN3 cells but not in the S cells. These results shown that transfected wt p53 confers multidrug sensitivity to HL-60 cells by re-adjustment of the expressions of apoptosis genes and displays other properties characteristic of endogenously originated wt p53.
Identifiers--KeyWord Plus(R): %TUMOR%-SUPPRESSOR GENE; ADENOVIRUS-MEDIATED

TRANSFER; %THERAPY% IN-VIVO; %CANCER% CELLS; CYCLE CONTROL; %THYMIDYLATE% SYNTHASE; NECK-%CANCER%; DNA-DAMAGE; BAX GENE; %EXPRESSION%

Cited References:

BAKER SJ, 1990, V249, P912, SCIENCE
BANERJEE D, 1995, V6, P1405, CELL GROWTH DIFFER
BJURSELL G, 1973, V248, P3904, J BIOL CHEM
BOOKSTEIN R, 1996, V23, P66, SEMIN ONCOL
CHEN XB, 1995, V55, P4257, CANCER RES
CLAYMAN GL, 1996, V122, P489, ARCH OTOLARYNGOL
CLEAVER JE, 1967, THYMIDINE METABOLISM
DELMASTRO DA, 1997, V39, P245, CANC CHEMOTHER PHARM
DUSENBERRY CE, 1990, V39, P285, MOL PHARMACOL
ELDEIRY WS, 1993, V75, P817, CELL
FAN SJ, 1994, V54, P5824, CANCER RES
FISHER DE, 1994, V72, P539, CELL
FUJIWARA T, 1994, V54, P2287, CANCER RES
FUJIWARA T, 1994, V86, P1458, J NATL CANCER I
GAVRIELI Y, 1992, V119, P493, J CELL BIOL
HAMADA K, 1996, V56, P3047, CANCER RES
HARPER JW, 1993, V75, P805, CELL
HARRIS CC, 1996, V88, P1442, J NATL CANCER I
HARTWELL LH, 1994, V266, P1821, SCIENCE
HEIDELBERGER C, 1983, V54, P58, ADV ENZYMOL
HORIKOSHI T, 1992, V52, P108, CANCER RES
JOHNSTON PG, 1995, V55, P1407, CANCER RES
KASTAN MB, 1996, V18, P617, BIOESSAYS
KINZLER KW, 1994, V331, P49, NEW ENGL J MED
KUFE DW, 1980, V64, P1307, CANCER TREAT REP
LEE JM, 1995, V14, P149, CANCER METAST REV
LESSONWOOD LA, 1995, V6, P395, HUM GENE THER
LINKE SP, 1996, V10, P934, GENE DEV
LIU TJ, 1994, V54, P3662, CANCER RES
LOWE SW, 1993, V74, P957, CELL
LOWE SW, 1994, V266, P807, SCIENCE
MIYASHITA T, 1995, V80, P293, CELL
MIYASHITA T, 1994, V9, P1799, ONCOGENE
NELSON WG, 1994, V14, P1815, MOL CELL BIOL
OLTVAI ZN, 1993, V74, P609, CELL
REED JC, 1994, V124, P1, J CELL BIOL
SEWING A, 1994, V9, P2733, ONCOGENE
SHAW P, 1992, V89, P4495, P NATL ACAD SCI USA
SMITH ML, 1996, V13, P2255, ONCOGENE
TAKAHASHI T, 1992, V52, P2340, CANCER RES
VISTICA DT, 1991, V51, P2515, CANCER RES
WEINBERG RA, 1995, V81, P323, CELL
WILLS KN, 1994, V5, P1079, HUM GENE THER
WOLF D, 1985, V82, P790, P NATL ACAD SCI USA
XIONG Y, 1993, V366, P701, NATURE
YANG B, 1996, V2, P1649, CLIN CANCER RES
YANG E, 1996, V88, P386, BLOOD
YONISHROUACH E, 1993, V13, P1415, MOL CELL BIOL
ZHAN QM, 1994, V9, P3743, ONCOGENE

11/5/3 (Item 3 from file: 34)

06619996 Genuine Article#: ZF220 Number of References: 24

Title: Higher levels of thymidylate synthase gene expression are observed in pulmonary as compared with hepatic metastases of colorectal adenocarcinoma

Author(s): Gorlick R; Metzger R; Danenberg KD; Salonga D; Miles JS; Longo GSA; Fu J; Banerjee D; Klimstra D; Jhanwar S; Danenberg PV; Kemeny N;

Bertino JR (REPRINT)
Corporate Source: MEM SLOAN KETTERING CANC CTR,DEPT PEDIAT, PROGRAM MOL PHARMACOL & THERAPEUT, 1275 YORK AVE, BOX 78/NEW YORK//NY/10021 (REPRINT); MEM SLOAN KETTERING CANC CTR,DEPT PEDIAT, PROGRAM MOL PHARMACOL & THERAPEUT/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT PATHOL/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT HUMAN GENET/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT MED/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT MOL PHARMACOL/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT EXPT THERAPEUT/NEW YORK//NY/10021; UNIV SO CALIF,KENNETH NORRIS JR COMPREHENS CANC CTR/LOS ANGELES//CA/90033
Journal: JOURNAL OF CLINICAL ONCOLOGY, 1998, V16, N4 (APR), P1465-1469
ISSN: 0732-183X Publication date: 19980400
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine;
Journal Subject Category: ONCOLOGY
Abstract: Purpose: It has been observed previously that the pulmonary metastases of colorectal adenocarcinoma are less responsive to therapy with fluorouracil (FUra) as compared with other sites of metastasis (liver, local). To investigate the basis of this chemoresistance, the levels of %thymidylate% synthase (TS) mRNA and protein were measured, as TS %expression% has been shown to be predictive of response to %therapy% in colorectal %cancer%.

Materials and Methods: Tumors were obtained from 19 patients with metastatic colorectal cancer(12 hepatic and seven pulmonary). TS expression was measured by quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) and TS protein levels were measured by Western blotting. The presence of TS amplification was assessed by Southern blotting. Levels of p53 protein were determined using immunohistochemistry.

Results: TS mRNA expression was shown to be significantly higher in the pulmonary metastases (mean TS/beta-actin ratio, 19.7; n = 7) as compared with the hepatic metastases (mean TS/beta-actin ratio, 4.7; n = 11) of colorectal cancer. Lower TS expression was observed in patients with hepatic metastases who had received prior FUra versus patients who had not been treated. High levels of TS expression in some samples was associated with low-level (two to three gene copies) increases in TS gene copy numbers and this was observed more frequently in the pulmonary metastatic samples. The increased gene copy numbers occurred both in samples with wild-type p53 and those with mutant p53 tumor-suppressor gene as determined by immunohistochemistry.

Conclusion: High levels of TS enzyme may be the basis of the lack of response of pulmonary metastases to FUra treatment. (C) 1998 by American Society of Clinical Oncology.
Identifiers--KeyWord Plus(R): WILD-TYPE P53; DIHYDROFOLATE-REDUCTASE; CANCER; AMPLIFICATION; RESISTANCE; SURVIVAL; QUANTITATION; PREDICTOR; CARCINOMA; TUMORS
Cited References:
BAAS IO, 1994, V172, P5, J PATHOL
BELLUCO C, 1996, V14, P2696, J CLIN ONCOL
BORING CC, 1993, V43, P7, CA-CANCER J CLIN
BRADFORD MM, 1976, V72, P248, ANAL BIOCHEM
DEGREGORI J, 1995, V15, P4215, MOL CELL BIOL
FAN J, 1997, V14, P1191, ONCOGENE
GIRARD P, 1996, V14, P2047, J CLIN ONCOL
GOKER E, 1995, V86, P677, BLOOD
HORIKOSHI T, 1992, V52, P108, CANCER RES
HUGHES K, 1989, V69, P340, SURG CLIN N AM

JOHNSTON PG, 1995, V55, P1407, CANCER RES
LEICHMAN L, 1995, V31, P1306, EUR J CANCER
LENZ HJ, 1996, V14, P176, J CLIN ONCOL
LI WW, 1992, V52, P1434, CANCER RES
LI WW, 1995, V92, P10436, P NATL ACAD SCI USA
LIVINGSTONE LR, 1992, V70, P923, CELL
MCCORMACK PM, 1979, V22, P553, DIS COLON RECTUM
MOERTEL CG, 1969, P122, ADV GASTROINTESTINAL
POON MA, 1989, V7, P1407, J CLIN ONCOL
RUSTUM YM, 1997, V15, P389, J CLIN ONCOL
SAMBROOK J, 1989, MOL CLONING LAB MANU
SOUTHERN EM, 1975, V98, P503, J MOL BIOL
WEISS L, 1986, V150, P195, J PATHOL
YIN YX, 1992, V70, P937, CELL

11/5/4 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05121552 Genuine Article#: BG03K Number of References: 69
Title: THE ROLE OF THYMIDYLATE SYNTHASE IN CELLULAR-REGULATION
Author(s): CHU E; ALLEGRA CJ
Corporate Source: NCI,USN,MED ONCOL BRANCH/BETHESDA//MD/20889
Journal: ADVANCES IN ENZYME REGULATION, 1996, V36, P143-163
ISSN: 0065-2571
Language: ENGLISH Document Type: REVIEW
Geographic Location: USA
Subfile: ISTP; SciSearch
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Identifiers--KeyWords Plus: COLON-CANCER-CELLS; TRANSFER-RNA SYNTHETASE; TUMOR-SUPPRESSOR GENE; KINASE MESSENGER-RNA; DIHYDROFOLATE-REDUCTASE; ESCHERICHIA-COLI; THYMIDINE KINASE; BINDING-SITE; MOUSE FIBROBLASTS; BREAST-CANCER
Research Fronts: 94-1131 004 (HIGH-DOSE 5-FLUOROURACIL 24-HOUR INFUSION; FOLINIC ACID; METASTATIC COLORECTAL-CARCINOMA; PHASE-II TRIAL; LEUCOVORIN %THERAPY%; HEPATIC ARTERIAL CHEMOTHERAPY)
94-6279 002 (P53 %TUMOR%-SUPPRESSOR GENE; EXHIBIT NORMAL G1 CELL-CYCLE ARREST; POSTTRANSLATIONAL REGULATION)
94-1893 001 (P53 PROTEIN; %EXPRESSION% IN MALIGNANT-MELANOMA; CARCINOGENESIS OF ESOPHAGEAL SQUAMOUS-CELL CARCINOMA)
94-5042 001 (%THYMIDYLATE% SYNTHASE; MOUSE WHEY ACIDIC PROTEIN PROMOTER HUMAN GROWTH-HORMONE (MWAP/HGH) TRANSGENIC MICE; HHAL METHYLTRANSFERASE FLIPS)
94-6508 001 (TRANSLATION INITIATION; REGULATION OF EIF-2 ALPHA-SUBUNIT PHOSPHORYLATION; S-ADENOSYLMETHIONINE DECARBOXYLASE MESSENGER-RNA; 5'-UNTRANSLATED REGION)
94-7136 001 (IRON-RESPONSIVE ELEMENT-BINDING PROTEIN; POSTTRANSCRIPTIONAL REGULATION; 3' UNTRANSLATED REGION; TRANSFERRIN RECEPTOR GENE-EXPRESSION)
Cited References:
ALEXANDER HR, 1995, V1, P49, CANCER J
ANDRAKE M, 1988, V85, P7942, P NATL ACAD SCI USA
AYUSAWA D, 1986, V190, P559, J MOL BIOL
BASTOW KF, 1984, V22, P15, ADV ENZYME REGUL
BERNARDI A, 1972, V69, P3033, P NATL ACAD SCI USA
BERNE MHO, 1986, V16, P237, CANCER CHEMOTH PHARM
BYSTROFF C, 1991, V30, P2227, BIOCHEMISTRY-US
CAREY J, 1983, V22, P2601, BIOCHEMISTRY-US
CHU E, 1993, V32, P4756, BIOCHEMISTRY-US
CHU E, 1990, V50, P5834, CANCER RES
CHU E, IN PRESS ADV CANC RE
CHU E, 1994, V269, P589, J BIOL CHEM
CHU E, 1994, V14, P207, MOL CELL BIOL
CHU E, 1995, V15, P179, MOL CELL BIOL

CHU E, 1991, V39, P136, MOL PHARMACOL
CHU E, 1993, V43, P527, MOL PHARMACOL
CHU E, 1995, V36, P3355, P AM ASSOC CANC RES
CHU E, 1991, V88, P8977, P NATL ACAD SCI USA
CHU E, 1993, V90, P517, P NATL ACAD SCI USA
COPUR S, 1995, V49, P1419, BIOCHEM PHARMACOL
COWAN KH, 1986, V30, P69, MOL PHARMACOL
CUNNINGHAM D, 1994, V13, P199, P AM SOC CLIN ONCOL
DANENBERG KD, 1989, V36, P219, MOL PHARMACOL
DANENBERG PV, 1977, V473, P73, BIOCHIM BIOPHYS ACTA
DAVIES JF, 1990, V29, P9467, BIOCHEMISTRY-US
DOMIN BA, 1982, V21, P478, MOL PHARMACOL
FRIEDKIN M, 1957, P609, CHEM BASIS HEREDITY
GOLD L, 1988, V57, P199, ANN REV BIOCH
HARDY LW, 1987, V235, P448, SCIENCE
HARRIS CC, 1993, V329, P1318, NEW ENGL J MED
HENDERSON BR, 1994, V269, P7481, J BIOL CHEM
HERSHEY JWB, 1991, V60, P717, ANN REV BIOCH
ITO M, 1990, V265, P6954, J BIOL CHEM
JENH CH, 1985, V122, P149, J CELL PHYSIOL
JOHNSTON PG, 1992, V52, P4306, CANCER RES
KASTAN MB, 1991, V51, P6304, CANCER RES
KEYOMARSI K, 1988, V263, P4402, J BIOL CHEM
KEYOMARSI K, 1993, V268, P5142, J BIOL CHEM
KLAUSNER RD, 1993, V72, P19, CELL
KNOFLER M, 1993, V268, P1409, J BIOL CHEM
KOONTZ SW, 1979, V254, P2277, J BIOL CHEM
KOZAK M, 1991, V266, P9867, J BIOL CHEM
LEARY RP, 1975, V250, P4864, J BIOL CHEM
LERNER MR, 1979, V76, P5495, P NATL ACAD SCI USA
LEVINE AJ, 1991, V351, P453, NATURE
MALTZMAN W, 1984, V4, P1689, MOL CELL BIOL
MELEFORS O, 1993, V15, P85, BIOESSAYS
MOERTEL CG, 1994, V330, P1136, NEW ENGL J MED
NAVALGUND LG, 1980, V255, P7386, J BIOL CHEM
PINEDO HM, 1988, V6, P1653, J CLIN ONCOL
PLESE PC, 1977, V252, P6139, J BIOL CHEM
PROKIPCAK RD, V269, P9261, J BIOL CHEM
ROMANIUK PJ, 1985, V24, P4239, BIOCHEMISTRY-US
SANTI DV, 1984, P345, FOLATES PTERINS
SATOS GA, 1994, V20, P11, CANC TREATMENT REV
SHERLEY JL, 1988, V263, P8350, J BIOL CHEM
SPEARS CP, 1982, V42, P450, CANCER RES
STARZYK RM, 1982, V298, P136, NATURE
STEITZ JA, 1989, V180, P468, METHOD ENZYMOL
SUIMADA Y, 1993, V11, P909, J CLIN ONCOL
SWAIN SM, 1989, V7, P890, J CLIN ONCOL
ULLRICH SJ, 1992, V267, P5259, J BIOL CHEM
VANDERWILT CL, 1992, V52, P4922, CANCER RES
VOGELSTEIN B, 1992, V70, P523, CELL
WASHTIEN WL, 1984, V25, P171, MOL PHARMACOL
WINTER RB, 1987, V84, P7822, P NATL ACAD SCI USA
WOLMARK N, 1993, V11, P1879, J CLIN ONCOL
YATES JL, 1980, V77, P1837, P NATL ACAD SCI USA
ZHAN QM, 1993, V13, P4242, MOL CELL BIOL

11/5/5 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04685417 Genuine Article#: UA994 Number of References: 66
Title: THE VOLE OF THYMIDYLATE SYNTHASE AS AN RNA-BINDING PROTEIN
Author(s): CHU E; ALLEGRA CJ
Corporate Source: USN,NCI,MED ONCOL BRANCH/BETHESDA//MD/20889

Journal: BIOESSAYS, 1996, V18, N3 (MAR), P191-198
ISSN: 0265-9247
Language: ENGLISH Document Type: REVIEW
Geographic Location: USA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: Thymidylate synthase plays a central role in the biosynthesis of thymidylate, an essential precursor for DNA biosynthesis. in addition to its role in catalysis and cellular metabolism, it is now appreciated that thymidylate synthase functions as an RNA binding protein. Specifically, thymidylate synthase binds with high affinity to its own mRNA, resulting in translational repression. An extensive series of experiments has been performed to elucidate the molecular elements underlying the interaction between thymidylate synthase and its own mRNA. In addition to characterization of the underlying cis- and trans-acting elements, recent studies have shown that thymidylate synthase has the capacity to bind specifically to other cellular RNA species. While the biological significance of these other RNA/thymidylate synthase interactions remains to be defined, this work suggests a potential role for TS in coordinately regulating several critical aspects of cellular metabolism.
Identifiers--KeyWords Plus: 3' UNTRANSLATED REGION; MESSENGER-RNA; ESCHERICHIA-COLI; NUCLEOTIDE-SEQUENCE; MOUSE FIBROBLASTS; R17-COAT PROTEIN; COAT PROTEIN; POLY(A) TAIL; CELL-LINE; TRANSLATION
Research Fronts: 94-1131 002 (HIGH-DOSE 5-FLUOROURACIL 24-HOUR INFUSION; FOLINIC ACID; METASTATIC COLORECTAL-CARCINOMA; PHASE-II TRIAL; LEUCOVORIN %THERAPY%; HEPATIC ARTERIAL CHEMOTHERAPY)
94-3689 002 (AU-RICH 3' UNTRANSLATED REGION OF MESSENGER-RNA; GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR %EXPRESSION%; RAT LIPOPOLYSACCHARIDE-BINDING PROTEIN)
94-5042 001 (%THYMIDYLATE% SYNTHASE; MOUSE WHEY ACIDIC PROTEIN PROMOTER HUMAN GROWTH-HORMONE (MWAP/HGH) TRANSGENIC MICE; HHAL METHYLTRANSFERASE FLIPS)
94-6279 001 (P53 %TUMOR%-SUPPRESSOR GENE; EXHIBIT NORMAL G1 CELL-CYCLE ARREST; POSTTRANSLATIONAL REGULATION)
94-7136 001 (IRON-RESPONSIVE ELEMENT-BINDING PROTEIN; POSTTRANSCRIPTIONAL REGULATION; 3' UNTRANSLATED REGION; TRANSFERRIN RECEPTOR GENE-EXPRESSION)
Cited References:
ANDRAKE M, 1988, V85, P7942, P NATL ACAD SCI USA
AYUSAWA D, 1986, V190, P559, J MOL BIOL
BELFORT M, 1983, V80, P4914, P NATL ACAD SCI USA
BERNARDI A, 1972, V69, P3033, P NATL ACAD SCI USA
CAREY J, 1983, V22, P2610, BIOCHEMISTRY-US
CAREY J, 1983, V22, P2601, BIOCHEMISTRY-US
CHU E, 1990, V50, P5834, CANCER RES
CHU E, 1994, V269, P289, J BIOL CHEM
CHU E, 1994, V14, P207, MOL CELL BIOL
CHU E, 1995, V15, P179, MOL CELL BIOL
CHU E, 1993, V43, P527, MOL PHARMACOL
CHU E, 1995, V36, P563, P AM ASSN CANC RES
CHU E, 1991, V88, P8977, P NATL ACAD SCI USA
CHU E, 1993, V90, P517, P NATL ACAD SCI USA
DANENBERG PV, 1977, V473, P73, BIOCHIM BIOPHYS ACTA
FRIEDKIN M, 1957, P609, CHEM BASIS HEREDITY
GALLIE DR, 1991, V5, P2108, GENE DEV
GEYER PK, 1984, V259, P7206, J BIOL CHEM
GOLD L, 1988, V57, P199, ANN REV BIOCH
HARDY LW, 1987, V235, P448, SCIENCE
HARRIS CC, 1993, V329, P1318, NEW ENGL J MED
HENDERSON BR, 1994, V269, P7481, J BIOL CHEM
JACKSON RJ, 1990, V62, P15, CELL
JACKSON RJ, 1993, V74, P9, CELL
JENH CH, 1985, V122, P149, J CELL PHYSIOL
JENH CH, 1985, V5, P2527, MOL CELL BIOL

KANEDA S, 1987, V15, P1259, NUCLEIC ACIDS RES
KANEDA S, 1987, V15, P1259, NUCLEIC ACIDS RES
KASTAN MB, 1991, V51, P6304, CANCER RES
KEYOMARSI K, 1988, V263, P4402, J BIOL CHEM
KEYOMARSI K, 1993, V268, P5142, J BIOL CHEM
KLAUSNER RD, 1993, V72, P19, CELL
KLAUSNER RD, 1989, V246, P870, SCIENCE
KOONTZ SW, 1979, V254, P2277, J BIOL CHEM
KOZAK M, 1991, V266, P9867, J BIOL CHEM
LEARY RP, 1975, V250, P4864, J BIOL CHEM
LEATHERS V, 1993, V13, P5331, MOL CELL BIOL
LERNER MR, 1979, V76, P5495, P NATL ACAD SCI USA
MCCARTHY JEG, 1995, V20, P191, TRENDS BIOCHEM SCI
MCELROY HE, 1992, V122, P265, J CRYST GROWTH
MELEFORS O, 1993, V15, P85, BIOESSAYS
NAVALGUND LG, 1980, V255, P7386, J BIOL CHEM
OSTARECKLEDERER A, 1994, V13, P1476, EMBO J
PLESE PC, 1977, V252, P6139, J BIOL CHEM
PROKIPCAK RD, 1994, V269, P9261, J BIOL CHEM
RAO KN, 1983, V80, P916, P NATL ACAD SCI USA
ROMANIUK PJ, 1985, V24, P4239, BIOCHEMISTRY-US
SANTI DV, 1984, V1, P345, FOLATES PTERINS
SCHIFFER CA, 1991, V219, P161, J MOL BIOL
SPEDDING G, 1993, V90, P4399, P NATL ACAD SCI USA
STARZYK RM, 1985, V298, P136, NATURE
STEITZ JA, 1989, V180, P468, METHOD ENZYMOL
SWAIN SM, 1989, V7, P890, J CLIN ONCOL
TAKEISHI K, 1985, V13, P2035, NUCLEIC ACIDS RES
THORNDIKE J, 1986, V139, P461, BIOCHEM BIOPH RES CO
TRIMBLE RB, 1976, V17, P538, J VIROL
TSAI DE, 1991, V19, P4931, NUCLEIC ACIDS RES
UHLENBECK OC, 1987, P285, MOL BIOL RNA NEW PER
VANDERWILT CL, 1992, V52, P4922, CANCER RES
VOELLER DM, 1995, V23, P869, NUCLEIC ACIDS RES
VOGELSTEIN B, 1992, V70, P523, CELL
WASHTIEN WL, 1984, V25, P171, MOL PHARMACOL
WINTER RB, 1987, V94, P7822, P NATL ACAD SCI USA
WU H, 1993, V32, P4761, BIOCHEMISTRY-US
YATES JL, 1980, V77, P1837, P NATL ACAD SCI USA
ZHAN QM, 1993, V13, P4242, MOL CELL BIOL

11/5/6 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03887805 Genuine Article#: QP339 Number of References: 42
Title: MESSENGER-RNA EXPRESSION OF RESISTANCE FACTORS AND THEIR CORRELATION TO THE PROLIFERATIVE ACTIVITY IN CHILDHOOD ACUTE LYMPHOBLASTIC-LEUKEMIA
Author(s): STAMMLER G; SAUERBREY A; VOLM M
Corporate Source: GERMAN CANC RES CTR,DEPT 0511,NEUENHEIMER FELD 280,POB 101949/D-69009 HEIDELBERG//GERMANY/; GERMAN CANC RES CTR,DEPT 0511/D-69009 HEIDELBERG//GERMANY/; UNIV JENA,CHILDRENS HOSP/O-6900 JENA//GERMANY/
Journal: CANCER LETTERS, 1995, V89, N1 (FEB 10), P129-135
ISSN: 0304-3835
Language: ENGLISH Document Type: ARTICLE
Geographic Location: GERMANY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: ONCOLOGY
Abstract: In this report we analyzed the mRNA expression of the resistance-related enzymes DNA topoisomerase II (Topo II), thymidylate synthase (TS), glutathione S-transferase-pi (GST-pi) and glutathione peroxidase (GP) in childhood acute lymphoblastic leukemia (ALL) and their correlation to the proliferative activity, determined by Ki-67.

RNA of blast cells from 54 children with untreated ALL were examined by dot blot hybridization. We found a significant positive correlation between Topo II and TS and cell proliferation. No significant correlation was detected between the mRNA expression of the glutathione-dependent enzymes GST-pi or GP and Ki-67. The results were substantiated by a semiquantitative RT-PCR-assay and by immunocytochemistry.

Descriptors--Author Keywords: DNA TOPOISOMERASE II ; THYMIDYLATE SYNTHASE ; GLUTATHIONE S-TRANSFERASE-PI ; GLUTATHIONE PEROXIDASE ; KI-67 ; PROLIFERATION ; ACUTE LYMPHOBLASTIC LEUKEMIA

Identifiers--KeyWords Plus: DNA TOPOISOMERASE-II; BREAST %CANCER%-CELLS; %THYMIDYLATE% SYNTHASE; %TUMOR%-CELLS; ELEVATED %EXPRESSION%; %DRUG% -RESISTANCE; ANTITUMOR DRUGS; PROGNOSIS; GENE; METHOTREXATE

Research Fronts: 93-3952 002 (MAMMALIAN DNA TOPOISOMERASE-II; ANTITUMOR AGENTS; POTENT INHIBITORS)

93-1657 001 (THYMIDYLATE SYNTHASE; PRENEOPLASTIC MAMMARY HYPERPLASTIC ALVEOLAR NODULES OF SHN VIRGIN MICE; 5-FLUOROURACIL GASTROINTESTINAL TOXICITY IN RATS)

93-1977 001 (GLUTATHIONE S-TRANSFERASES; ADULT TOAD (BUFO-BUFO) LIVER; MAMMALIAN THETA-CLASS ISOENZYMES)

93-3155 001 (PROLIFERATING CELL NUCLEAR ANTIGEN; PROGNOSTIC IMPACT IN ARCHIVAL PARAFFIN-EMBEDDED NODE-NEGATIVE BREAST-CANCER; IMMUNOHISTOCHEMICAL EVIDENCE)

Cited References:

BATIST G, 1986, V261, P5544, J BIOL CHEM
BERGER SH, 1985, V28, P461, MOL PHARMACOL
BUTLER RN, 1994, V9, P60, J GASTROEN HEPATOL
CADMAN E, 1986, V46, P1195, CANCER RES
CHOMCZYNSKI P, 1987, V162, P156, ANAL BIOCHEM
CRESPI MD, 1986, V136, P521, BIOCHEM BIOPH RES CO
CROWTHER D, 1975, V32, P456, BRIT J CANCER
CURT GA, 1985, V76, P1323, J CLIN INVEST
DANENBERG PV, 1977, V473, P73, BIOCHIM BIOPHYS ACTA
DOW LW, 1982, V59, P1197, BLOOD
DREWINKO B, 1981, V41, P2328, CANCER RES
ELLEDGE RM, 1994, V8, P67, MOL CELL PROBE
ESTRELA JM, 1992, V286, P257, BIOCHEM J
FOADI M, 1968, V15, P269, BRIT J HAEMATOL
GEKELER V, 1992, V66, P507, BRIT J CANCER
GERDES J, 1991, V138, P867, AM J PATHOL
GIORDANO M, 1992, V71, P2739, CANCER
HART JS, 1977, V39, P1603, CANCER
JENH CH, 1985, V122, P149, J CELL PHYSIOL
LI WW, 1992, V52, P3908, CANCER RES
LING V, 1983, V67, P869, CANCER TREAT REP
LIU LF, 1989, V58, P351, ANNU REV BIOCHEM
MATTERN J, 1993, V2, P557, INT J ONCOL
MURPHY SB, 1977, V49, P683, BLOOD
PONTE P, 1984, V12, P1687, NUCLEIC ACIDS RES
PORRECA E, 1993, V100, P141, ATHEROSCLEROSIS
POTMESIL M, 1988, V48, P3537, CANCER RES
RICCARDI A, 1991, V27, P882, EUR J CANCER
ROSS W, 1984, V44, P5857, CANCER RES
SAUERBREY A, 1994, IN PRESS BR J CANCER
SCANLON KJ, 1988, V85, P650, P NATL ACAD SCI USA
SCARFFE JH, 1980, V41, P764, BRIT J CANCER
SILBER R, 1989, V29, P267, ADV ENZYME REGUL
SINHA BK, 1989, V1010, P304, BIOCHIM BIOPHYS ACTA
STAMMLER G, 1994, V84, P141, CANCER LETT
SULLIVAN DM, 1986, V25, P2248, BIOCHEMISTRY-US
TEWEY KM, 1984, V259, P9182, J BIOL CHEM
TIEDEFELD U, 1992, V52, P3281, CANCER RES
TSAIPFLUGFELDER M, 1988, V85, P7177, P NATL ACAD SCI USA
VOLM M, 1992, V12, P2293, ANTICANCER RES
VOLM M, 1994, V14, P1377, ANTICANCER RES

. WOESSNER RD, 1991, V2, P209, CELL GROWTH DIFFER

11/5/7 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02050030 Genuine Article#: JW768 Number of References: 106
Title: DRUG-RESISTANCE IN ONCOLOGY - FROM CONCEPTS TO APPLICATIONS
Author(s): CAZIN JL; GOSSELIN P; CAPPELAERE P; ROBERT J; DEMAILLE A
Corporate Source: CTR OSCAR LAMBRET,RADIOPHARM & ONCOPHARMACOL LAB,1 RUE F COMBEMALE,BP 307/F-59020 LILLE//FRANCE/; FDN BERGONIE,BIOCHIM LAB/F-33076 BORDEAUX//FRANCE/
Journal: JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, 1992, V119, N2 (NOV), P76-86
ISSN: 0171-5216
Language: ENGLISH Document Type: EDITORIAL
Geographic Location: FRANCE
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: ONCOLOGY
Abstract: The complex problem of drug resistance is discussed with respect to host toxicity, to tumor characteristics (kinetic resistance, heterogeneity of cell subpopulations, hypoxia, mutation and gene amplification), and to the medication itself (pharmacokinetic and pharmacodynamic resistance: cell membrane, intracellular metabolism, intracellular target). After detailing each type of resistance, the possibilities of fighting against drug resistance are explored (dealing with host toxicity, tumor characteristics and drugs - intensifying therapy, multiple drug therapy, biochemical modulation, particular modalities of drug administration). Finally, perspectives of research and development of new drugs are summarized.
Descriptors--Author Keywords: ONCOPHARMACOLOGY ; RESISTANCE TO CHEMOTHERAPY ; PGP ; GST ; TOPOISOMERASES
Identifiers--KeyWords Plus: BACTERIAL TRANSPORT PROTEINS; P-GLYCOPROTEIN EXPRESSION; DOUBLE MINUTE CHROMOSOMES; CANCER CELL-LINES; MULTIDRUG-RESISTANCE; MONOCLONAL-ANTIBODIES; ANTICANCER DRUGS; LEUKEMIA-CELLS; CYTO-TOXICITY; CONFERS RESISTANCE
Research Fronts: 90-0790 012 (MULTIDRUG RESISTANCE; P-GLYCOPROTEIN %EXPRESSION%; ACTIVITY OF VERAPAMIL)
90-2128 001 (%THYMIDYLATE% SYNTHASE; CONTINUOUS INFUSION HIGH-DOSE LEUCOVORIN; 5-FLUOROURACIL ACTIVITY; FOLINIC ACID; COLON %CANCER%)
90-2380 001 (PHOTODYNAMIC %THERAPY%; %TUMOR% FACTORS IN CANCER METASTASIS; HEMATOPORPHYRIN DERIVATIVE; INVIVO GROWTH)
90-3635 001 (MOLECULAR EVOLUTION OF THE ESCHERICHIA-COLI CHROMOSOME; HOMOLOGOUS RECOMBINATION; ADAPTIVE MUTATIONS; BACTERIAL OPERON; RIF-1 TUMORS; CANCER METASTASIS)
90-6024 001 (CHEMOTHERAPY OF HODGKINS-DISEASE; LIMITED STAGE SMALL-CELL LUNG-CANCER; NO MAINTENANCE THERAPY)
90-6295 001 (CISPLATIN RESISTANCE; DNA INTERACTIVE ANTICANCER DRUGS; REDUCED GLUTATHIONE; HUMAN OVARIAN-CARCINOMA CELLS; N-15-[H-1] DEPT NMR)
Cited References:
ALBRECHT AM, 1984, P317, FOLATE ANTAGONISTS T
ALT FW, 1978, V253, P1351, J BIOL CHEM
ARMAND JP, 1986, P193, THERAPEUTIQUE CANCER
BAGULEY BC, 1990, V82, P398, J NATL CANCER I
BECHHANSEN NT, 1976, V88, P23, J CELL PHYSIOL
BECK WT, 1990, V77, P1131, B CANCER
BECK WT, 1987, V47, P5455, CANCER RES
BENET LZ, 1990, P3, PHARMACOL BASIS THER
BIEDLER J, 1971, V191, P185, SCIENCE
BIEDLER JL, 1970, V30, P1174, CANCER RES
BROWN JM, 1979, V52, P650, BRIT J RADIOL
BROWN JM, 1990, V82, P338, J NATL CANCER I
BUNGO M, 1990, V50, P2549, CANCER RES

CABRAL F, 1980, V20, P29, CELL
CALVERT AH, 1989, V8, P493, CANCER SURV
CALVO F, 1989, P211, MARQUEURS TUMORAUX P
CAZIN JL, 1991, V10, P45, J PHARM CLIN
CENCIARELLI C, 1991, V47, P533, INT J CANCER
CHEN CJ, 1986, V47, P381, CELL
COLEMAN CN, 1989, P2436, CANCER PRINCIPLES PR
CONNORS TA, 1989, V8, P693, CANCER SURV
CURT GA, 1983, V308, P199, NEW ENGL J MED
DEISSEROTH AB, 1989, P2413, CANCER PRINCIPLES PR
DEVITA VT, 1991, V2, P93, ANN ONCOL
DEVITA VT, 1990, P7, DRUG RESISTANCE MECH
DHIR R, 1990, V77, P1125, B CANCER
DINCALCI M, 1988, V15, P279, CANCER TREAT REV
ENDRESEN L, 1984, V55, P183, ACTA PHARMACOL TOX
EPSTEIN RJ, 1990, V8, P2062, J CLIN ONCOL
ERLICHMAN C, 1988, V6, P469, J CLIN ONCOL
FABRE I, 1984, V44, P3190, CANCER RES
FINE RL, 1989, P107, DRUG RESISTANCE CANC
FITZGERALD DJ, 1987, V84, P4288, P NATL ACAD SCI USA
FOOTE SJ, 1990, V345, P255, NATURE
FORD JM, 1990, V42, P155, PHARMACOL REV
FUQUA SAW, 1988, P45, CANCER CHEMOTHERAPY
GENNIS RB, 1989, BIOMEMBRANES MOL STR
GERLACH JH, 1986, V324, P485, NATURE
GOLDIE JH, 1979, V44, P3643, CANCER RES
GOLDIE JH, 1982, V66, P439, CANCER TREAT REP
GOLDIN A, 1989, P1, RESISTANCE ANTINEOPL
GOLDSTEIN LJ, 1991, P101, MOL CLIN ADV ANTICAN
GOTTESMAN MM, 1989, V7, P409, J CLIN ONCOL
GOTTESMAN MM, 1988, V9, P54, TRENDS PHARMACOL SCI
GROS P, 1986, V47, P371, CELL
GROS P, 1986, V323, P728, NATURE
GRUNBERG SM, 1990, V322, P846, NEW ENGL J MED
HAMADA H, 1989, V50, P3167, CANCER RES
HAMADA H, 1986, V83, P7785, P NATL ACAD SCI USA
HEPPNER GH, 1984, V44, P2259, CANCER RES
HERWEIJER H, 1990, V82, P1133, J NATL CANCER I
HRUSHESKY WJM, 1985, V228, P73, SCIENCE
HRYNIUK WM, 1989, P121, CANCER PRINCIPLES PR
HRYNIUK WM, 1987, V14, P65, SEMIN ONCOL
HU XF, 1990, V50, P2953, CANCER RES
JULIANO RL, 1976, V455, P152, BIOCHIM BIOPHYS ACTA
KARTNER N, 1985, V316, P820, NATURE
KARTNER N, 1983, V221, P1285, SCIENCE
KAUFMAN RJ, 1979, V76, P5669, P NATL ACAD SCI USA
KELLEN JA, 1991, V11, P917, ANTICANCER RES
KELLEY SL, 1988, V241, P1813, SCIENCE
KUWAZURU Y, 1990, V76, P2065, BLOOD
LAI GM, 1989, V81, P535, J NATL CANCER I
LAW LW, 1952, V169, P628, NATURE
LING V, 1973, V83, P103, J CELL PHYSL
LIU LF, 1990, P251, DRUG RESISTANCE MECH
LURIA SE, 1943, V28, P491, GENETICS
MA DDF, 1989, V19, P736, AUST NZ J MED
MARTY M, 1990, V322, P816, NEW ENGL J MED
MCLACHLIN JR, 1990, V82, P1260, J NATL CANCER I
MEYERS MB, 1989, V49, P3209, CANCER RES
MUGGIA FM, 1990, P331, DRUG RESISTANCE MECH
MUSTO P, 1991, V77, P50, BRIT J HAEMATOL
OHNOSHI T, 1982, V42, P1655, CANCER RES
OZOLS RF, 1987, V36, P147, BIOCHEM PHARMACOL
PASTAN I, 1991, V42, P277, ANNU REV MED
PASTAN I, 1987, V316, P1388, NEW ENGL J MED
PENNOCK GD, 1991, V83, P105, J NATL CANCER I

PHILLIPS RM, 1990, V82, P1457, J NATL CANCER I
POUPON MF, 1990, V4, P49, CANCER COMMUN
POUPON MF, 1989, V37, P1018, PATHOL BIOL
POWIS G, 1990, V50, P2203, CANCER RES
PRICE JE, 1990, V66, P1313, CANCER
RETSKY MW, 1987, V47, P4982, CANCER RES
RIORDAN JR, 1985, V376, P817, NATURE
ROBERT J, 1990, V77, P1124, B CANCER
ROSEN G, 1986, P103, METHOTREXATE CANCER
ROTHENBERG M, 1989, V81, P907, J NATL CANCER I
ROWLAND M, 1989, CLIN PHARMACOKINETIC
RUSTUM YM, 1990, P89, DRUG RESISTANCE MECH
SARTORELLI AC, 1988, V48, P775, CANCER RES
SCANLON KJ, 1986, V83, P8923, P NATL ACAD SCI USA
SCHEPER RJ, 1988, V42, P389, INT J CANCER
SINGER SJ, 1972, V175, P720, SCIENCE
SKIPPER HE, 1950, V54, P431, CANCER CHEMOTH REP
SKIPPER HE, 1961, V21, P1154, CANCER RES
STORB R, 1989, P2474, CANCER PRINCIPLES PR
TANNOCK IF, 1989, P3, CANCER PRINCIPLES PR
TATTERSALL MH, 1974, V27, P39, BRIT J HAEMATOL
TRENT JM, 1984, V2, P8, J CLIN ONCOL
TSURUO T, 1981, V41, P1967, CANCER RES
TUBIANA M, 1973, V21, P647, PATHOL BIOL
UEDA K, 1987, V84, P3004, P NATL ACAD SCI USA
VAUPEL P, 1989, V49, P6449, CANCER RES
WORKMAN P, 1990, V1, P100, ANN ONCOL
YOUNG RC, 1989, P1, DRUG RESISTANCE CANC

11/5/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09745479 BIOSIS NO.: 199598200397
Alteration of metallothionein or %thymidylate% synthase %expression% in human %tumor% cells: Effects on %drug% resistance.
AUTHOR: Demoor J; Koropatnick J; Vincent M; Sharpe J; Vertesi V; Collins O; Leibbrandt M; Fraser J
AUTHOR ADDRESS: London Regional Cancer Centre, London N6A 4L6**Canada
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 36 (0):p321 1995
CONFERENCE/MEETING: Eighty-sixth Annual Meeting of the American Association for Cancer Research Toronto, Ontario, Canada March 18-22, 1995
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 9031-61-2: THYMIDYLATE SYNTHASE; 15663-27-1: CISPLATIN; 305-03-3: CHLORAMBUCIL; 7440-43-9: CADMIUM
DESCRIPTORS:
MAJOR CONCEPTS: Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Oncology (Human Medicine, Medical Sciences); Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Hominidae (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
CHEMICALS & BIOCHEMICALS: THYMIDYLATE SYNTHASE; CISPLATIN; CHLORAMBUCIL ; CADMIUM
MISCELLANEOUS TERMS: ANTINEOPLASTIC-DRUG; CADMIUM; CHLORAMBUCIL; CISPLATIN; DRUG RESISTANCE MECHANISMS; IONIZING RADIATION; MEETING ABSTRACT; METAL HOMEOSTASIS
CONCEPT CODES:
10808 Enzymes-Physiological Studies
13010 Metabolism-Minerals

22002 Pharmacology-General
24006 Neoplasms and Neoplastic Agents-Biochemistry
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
02506 Cytology and Cytochemistry-Animal
06504 Radiation-Radiation and Isotope Techniques
06506 Radiation-Radiation Effects and Protective Measures
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10069 Biochemical Studies-Minerals
BIOSYSTEMATIC CODES:
86215 Hominidae

11/5/9 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09856197 98384332 PMID: 9716444
Antisense nucleic acids targeted to the thymidylate synthase (TS) mRNA translation start site stimulate TS gene transcription.
DeMoor JM; Vincent MD; Collins OM; Koropatnick J
The London Regional Cancer Centre, 790 Commissioners Road East, London, Ontario, N6A 4L6, Canada.
Experimental cell research (UNITED STATES) Aug 25 1998, 243 (1) p11-21, ISSN 0014-4827 Journal Code: EPB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Thymidylate synthase (TS) is a key enzyme in the synthesis of DNA and a target for cancer chemotherapeutic agents. Antisense TS nucleic acids may be useful in enhancing anticancer drug effectiveness. MCF-7 and HeLa cells were transfected with vectors expressing antisense TS RNA or with antisense oligodeoxynucleotides (AS-ODNs) to different TS mRNA regions. Antisense RNAs were targeted to 30 bases of the TS mRNA including part of the stem loop at the translation start site and to 30 bases spanning the exon1/exon2 boundary. AS-ODNs were targeted to the translation start site and the translation stop site. Antisense nucleic acids complementary to the translation start site (and not the exon1/exon2 boundary or translation stop site) significantly enhanced constitutive TS gene transcription. Therefore, TS mRNA sequences appear to be involved in a novel pathway controlling TS gene transcription. Induced transcription could hinder antisense-based attempts to inhibit TS and must be considered when designing such strategies. Copyright 1998 Academic Press.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *RNA, Antisense--pharmacology--PD; *Thymidylate Synthase --genetics--GE; Blotting, Northern; Blotting, Southern; Breast Neoplasms --genetics--GE; Breast Neoplasms--metabolism--ME; Down-Regulation (Physiology); Gene %Expression%--%drug% effects--DE; Hela Cells--metabolism --ME; Oligonucleotides, Antisense--pharmacology--PD; RNA, Messenger --analysis--AN; %Thymidylate% Synthase--%drug% effects--DE; Transcription, Genetic--%drug% effects--DE; Transfection; %Tumor% Cells, Cultured
CAS Registry No.: 0 (Oligonucleotides, Antisense); 0 (RNA, Antisense) ; 0 (RNA, Messenger)
Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)
Record Date Created: 19980924

11/5/10 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09792875 98324629 PMID: 9662252
Thymidylate synthase expression and activity: relation to S-phase

parameters and 5-fluorouracil sensitivity.
Mirjolet JF; Barberi-Heyob M; Merlin JL; Marchal S; Etienne MC; Milano G; Bey P
Centre Alexis Vautrin, Laboratoire de Recherche en Oncologie, Vandoeuvre-les-Nancy, France.
British journal of cancer (SCOTLAND) Jul 1998, 78 (1) p62-8, ISSN 0007-0920 Journal Code: AV4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Six human cancer cell lines exhibiting a large range of sensitivity to 5-fluorouracil (5-FU) were evaluated for thymidylate synthase (TS) and p53 gene expression, TS and dihydropyrimidine dehydrogenase (DPD) activity, as well as cell cycle parameters, S-phase fraction (SPF), bromodeoxyuridine labelling index (LI) and S-phase duration (SPD). All these parameters were investigated for 7 days in asynchronously growing cell populations and compared with the cell sensitivity to 5-FU. No significant correlation was found between S-phase parameters and TS gene expression and/or activity. TS activity was higher in proliferating cells; however, it was not significantly higher in rapidly growing cell lines with short SPD. Neither TS gene expression nor activity was found to correlate with 5-FU sensitivity. On the another hand, a statistically significant correlation ($P < 0.0001$) was observed between LI and SPD and 5-FU sensitivity. The present results suggest that cell cycle parameters such as SPD and/or LI could be better parameters for 5-FU sensitivity prediction than TS gene expression and/or activity. This could be especially informative in cases of concomitant radio-chemotherapy as S-phase parameters are already proposed for hyperfractionated radiotherapy planning.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *Antimetabolites, Antineoplastic--pharmacology--PD; *Fluorouracil--pharmacology--PD; *Neoplasm Proteins--metabolism--ME; *S Phase--physiology--PH; *Thymidylate Synthase--metabolism--ME; Cell Division --%drug% effects--DE; Gene %Expression% Regulation, Enzymologic; Neoplasm Proteins--genetics--GE; Oxidoreductases--metabolism--ME; %Thymidylate% Synthase--genetics--GE; %Tumor% Cells, Cultured--%drug% effects--DE
CAS Registry No.: 0 (Antimetabolites, Antineoplastic); 0 (Neoplasm Proteins); 51-21-8 (Fluorouracil)
Enzyme No.: EC 1. (Oxidoreductases); EC 1.3.1.2 (dihydrouracil dehydrogenase(NADP)); EC 2.1.1.45 (Thymidylate Synthase)
Record Date Created: 19980720

11/5/11 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09401651 97309778 PMID: 9167189
Determinants of cytotoxicity with prolonged exposure to fluorouracil in human colon cancer cells.
Ren Q; Van Groeningen CJ; Hardcastle A; Aherne GW; Geoffroy F; Allegra CJ ; Johnston PG; Grem JL
Developmental Therapeutics Department, National Cancer Institute, National Naval Medical Center, Bethesda, MD 20889-5105, USA.
Oncology research (UNITED STATES) 1997, 9 (2) p77-88, ISSN 0965-0407 Journal Code: BBN
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
To explore the determinants of cytotoxicity during prolonged exposure to pharmacologically relevant concentrations of 5-fluorouracil (FUra), we studied the effects of FUra at concentrations ranging from 0.1 to 1 microM in HCT 116 and HT 29 colon cancer cells grown in the presence of physiologic levels of leucovorin. A 5- and 7-day exposure to 1 microM FUra

reduced cell growth to 46% and 20% of control in HT 29 cells and to 74% and 38% of control in HCT 116 cells. Concurrent exposure to thymidine (10 or 20 microM) or uridine (1 mM) provided partial protection against FUra toxicity in HT 29 cells, but did not protect HCT 116 cells. After a 24-h exposure to 1 microM [3H]FUra, free 5-fluoro-2'-deoxyuridine-5' -monophosphate (FdUMP) and FUDP. + FUTP levels were 0.7 and 144 pmol/10(6) cells in HT 29 cells, respectively, and 3.9 and 178 pmol/10(6) cells in HCT 116 cells. FdUMP and FUDP + FUTP pools increased by 5.7- and 2.0-fold in HT 29 cells and by 1.7- and 3.3-fold in HCT 116 cells over the next 48 h, but did not accumulate thereafter. After a 24-h exposure to 1 microM [3H]FUra, FUra-RNA levels were 158 and 280 fmol/microgram in HT 29 and HCT 116 cells, respectively; FUra-RNA levels increased over time, and reached 700 and 1156 fmol/microgram at day 5. Concurrent exposure to 1 mM uridine for 72 h did not diminish [3H]FUra-RNA incorporation. Upon removal of [3H]FUra following a 24-h exposure, FUra-RNA levels remained relatively stable with 57-78% retained at 120 h. A low level of [3H]FUra-DNA incorporation was detected in HT 29 cells. Thymidylate synthase (TS) catalytic activity in control cells was 2-fold higher in HCT 116 cells compared to HT 29 cells (47 vs. 23 pmol/min/mg). Total TS content increased 1.5- to 3-fold over control in both cell lines during FUra exposure, and ternary complex formation was evident for up to 96 h-dTTP pools were not depleted in FUra-treated cells, suggesting that residual TS catalytic activity was sufficient to maintain dTTP pools relative to demand. Surprisingly, the partial inhibition of TS was accompanied by a striking accumulation of immunoreactive "dUMP" pools in both lines; dUTP pools also increased 2-to 3-fold. In summary, the gradual and stable accumulation of FUra in RNA noted in both lines may account for the thymidine-insensitive component of FUra toxicity. Because dTTP pools were not appreciably diminished, the interference with nascent DNA chain elongation and induction of single-strand breaks in newly synthesized DNA in both cell lines may be due to misincorporation of deoxyuridine nucleotides.

Tags: Human

Descriptors: *Cell Survival--drug effects--DE; *DNA Damage; *Fluorouracil --toxicity--TO; *Leucovorin--pharmacology--PD; Cell Division--drug effects --DE; Colonic Neoplasms; DNA, Neoplasm--%drug% effects--DE; Deoxyribonucleotides--metabolism--ME; Deoxyuracil Nucleotides--metabolism --ME; Dose-Response Relationship, %Drug%; Fluorodeoxyuridylate--metabolism --ME; Fluorouracil--metabolism--ME; Gene %Expression% Regulation, Enzymologic--%drug% effects--DE; %Thymidylate% Synthase--antagonists and inhibitors--AI; %Thymidylate% Synthase--biosynthesis--BI; %Tumor% Cells, Cultured; Uridine Triphosphate--analogs and derivatives--AA; Uridine Triphosphate--metabolism--ME

CAS Registry No.: 0 (5-fluoro-2'-deoxyuridine-5'-diphosphate); 0 (DNA, Neoplasm); 0 (Deoxyribonucleotides); 0 (Deoxyuracil Nucleotides); 134-46-3 (Fluorodeoxyuridylate); 3828-96-4 (5-fluorouridine 5'-triphosphate); 51-21-8 (Fluorouracil); 58-05-9 (Leucovorin); 63-39-8 (Uridine Triphosphate)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19970710

11/5/12 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08766826 95226450 PMID: 7711067

Isolation and expression of rat thymidylate synthase cDNA: phylogenetic comparison with human and mouse thymidylate synthases.

Ciesla J; Weiner KX; Weiner RS; Reston JT; Maley GF; Maley F

Nencki Institute of Experimental Biology, Department of Cellular Biochemistry, Warsaw, Poland.

Biochimica et biophysica acta (NETHERLANDS) Apr 4 1995, 1261 (2) p233-42, ISSN 0006-3002 Journal Code: A0W

Contract/Grant No.: CA44355, CA, NCI

Languages: ENGLISH

Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS

Two cDNA clones representing rat hepatoma thymidylate synthase (rTS) were isolated from a lambda ZAP II cDNA library using as a probe a fragment of the human TS cDNA. The two were identical except that one was missing 50 bp and the other 23 bp corresponding to the 5' coding region of the protein. The missing region was obtained by screening a rat genomic library. The open reading frame of rTS cDNA encoded 921 bp encompassing a protein of 307 amino acids with a calculated molecular mass of 35,015 Da. Rat hepatoma TS appears identical to normal rat thymus TS and the two sequences differ from mouse TS in the same eight amino acid residues. Six of these differences are in the first 21 amino acids from the amino-end. The human enzyme differed from rat and mouse TS at 17 residues where the latter two were identical, with most changes being conservative in nature. The three species differed completely at only four sites. Because the mouse TS shares four amino acids with human TS at sites which differ from rTS and a comparable situation does not exist between rTS and human TS, it is suggested that mouse TS is closer to human TS phylogenetically than rTS. The polymerase chain reaction was used to subclone the protein coding region of rTS into a high expression vector, which expressed rTS in Escherichia coli to the extent of 10 to 20% of its cellular protein. Although the amino-end of the amplified TS was unblocked, that isolated from a FUdR-resistant rat hepatoma cell line contained mostly N-acetylmethionine on its N-terminal end, a finding that may have significant regulatory consequences, which are discussed. The TS level in the resistant cell line was 60 to 70-fold higher than normal which was found to be associated with both multiple gene copies and an expanded TS mRNA pool.

Tags: Animal; Comparative Study; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *DNA, Complementary--isolation and purification--IP; *Thymidylate Synthase--genetics--GE; Amino Acid Sequence; Base Sequence; Carcinoma, Hepatocellular--genetics--GE; Cloning, Molecular; DNA, Complementary--metabolism--ME; %Drug% Resistance; Escherichia coli --metabolism--ME; Gene %Expression%; Mice; Molecular Sequence Data; Rats; Recombinant Proteins--genetics--GE; %Thymidylate% Synthase--metabolism--ME; %Tumor% Cells, Cultured

Molecular Sequence Databank No.: GENBANK/L12138
CAS Registry No.: 0 (DNA, Complementary); 0 (Recombinant Proteins)
Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)
Record Date Created: 19950515

11/5/13 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08550725 95326357 PMID: 7602796
Rapid diagnosis of drug-resistant genes by PCR assay.
Funato T
Department of Clinical and Laboratory Medicine, Tohoku University School of Medicine, Sendai.
Rinsho byori (JAPAN) Jun 1995, 43 (6) p535-9, ISSN 0047-1860
Journal Code: KIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS

This report concerns the utility of the reverse transcription-polymerase chain reaction (RT-PCR) and quantitative PCR (QPCR) assay to detect the %drug%-resistance of related genes. The expression of some %drug% -resistance genes was compared with the sensitivity and resistance-acquired %cancer% cell lines to anti-%cancer% drugs by Northern blot analysis and PCR assay. The resistance cell lines exhibited an enhanced %expression% of

multi-%drug% resistance (MDR-1), %thymidylate% synthase (TS), c-fos and DNA polymerase beta genes. Then these genes that %expressed% mRNA were quantitated using RT-PCR. The expression of the genes was dependent on their sensitivity (IC50) to anti-%cancer% drugs. Additionally, the QPCR assay has been developed as a rapid method for the expression of %drug% -resistance genes and applied to the PCR products amplified by the RT-PCR. Thus the QPCR assay for the expression of genes will allow rapid detection of the drug-resistance to chemotherapy in human cancers.

Tags: Human

Descriptors: *Drug Resistance--genetics--GE; Blotting, Northern; Drug Resistance, Multiple--genetics--GE; Polymerase Chain Reaction--methods--MT

Record Date Created: 19950808

11/5/14 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08033613 93233612 PMID: 8474431

Regulation of thymidylate synthase in human colon cancer cells treated with 5-fluorouracil and interferon-gamma.

Chu E; Koeller DM; Johnston PG; Zinn S; Allegra CJ

NCI-Navy Medical Oncology Branch, Bethesda, Maryland 20889.

Molecular pharmacology (UNITED STATES) Apr 1993, 43 (4) p527-33, ISSN 0026-895X Journal Code: NGR

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

The effects of fluorouracil (5-FU) and interferon-gamma (IFN-gamma) on the regulation of thymidylate synthase (TS) gene expression were investigated in the human colon cancer H630 cell line. By Western immunoblot analysis, TS protein levels in H630 cells were increased 3-, 5.5-, 5-, and 2.5-fold after 8-, 16-, 24-, and 36-hr exposure to 1 microM 5-FU, respectively. When H630 cells were exposed to varying concentrations of 5-FU (0.3-10 microM) for 24 hr, increases in TS protein up to 5.5-fold were observed. A 24-hr exposure to 1 microM 5-FU resulted in a 4.5-fold increase in the level of TS protein, whereas in 5-FU/IFN-gamma-treated cells TS protein was increased by only 1.8-fold, compared with control cells. IFN-gamma treatment alone did not affect TS protein levels, relative to control. Northern blot analysis revealed no changes in TS mRNA levels when H630 cells were exposed either to 1 microM 5-FU for 8-36 hr, to varying concentrations of 5-FU (0.3-10 microM) for 24 hr, or to the combination of 5-FU and IFN-gamma. Pulse-labeling studies with [35S]methionine demonstrated a 3.5-fold increase in net synthesis of TS in cells treated with 1 microM 5-FU, whereas the level of newly synthesized TS increased only 1.5-fold in cells treated with 5-FU/IFN-gamma, compared with control cells. Pulse-chase studies revealed that the half-lives of TS protein in control and 5-FU-treated cells were equivalent. These findings demonstrate that the increase in TS protein after 5-FU exposure and the subsequent inhibitory effect of IFN-gamma on TS protein expression are both regulated at the post-transcriptional level.

Tags: Human

Descriptors: *Colonic Neoplasms--enzymology--EN; *Fluorouracil --pharmacology--PD; *Interferon Type II--pharmacology--PD; *Thymidylate Synthase--drug effects--DE; %Drug% Synergism; Enzyme Induction--%drug% effects--DE; Enzyme Stability--%drug% effects--DE; Gene %Expression% Regulation, Neoplastic--%drug% effects--DE; RNA, Messenger--%drug% effects --DE; RNA, Neoplasm--%drug% effects--DE; %Thymidylate% Synthase --biosynthesis--BI; %Thymidylate% Synthase--genetics--GE; Translation, Genetic--%drug% effects--DE; %Tumor% Cells, Cultured

CAS Registry No.: 0 (RNA, Messenger); 0 (RNA, Neoplasm); 51-21-8 (Fluorouracil); 82115-62-6 (Interferon Type II)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19930518

11/5/15 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06911534 93090888 PMID: 1457523
Antimetabolites.
Chen AP; Grem JL
National Cancer Institute, Bethesda, Maryland.
Current opinion in oncology (UNITED STATES) Dec 1992, 4 (6) p1089-98
, ISSN 1040-8746 Journal Code: A1V
Languages: ENGLISH
Document type: Journal Article; Review; Review Literature
Record type: Completed
Subfile: INDEX MEDICUS
Research efforts over the past year further elucidate the determinants of sensitivity and mechanisms of resistance to the antimetabolites fluorouracil, methotrexate, and cytarabine. Progress has been made in clarifying the complex regulation of target enzyme %expression% for these antimetabolites. Advances in analytical methodology should facilitate quantitation of %thymidylate% synthase content in %tumor% tissue prior to and following fluorouracil-based %therapy% . Information concerning the basis for certain %drug% interactions may guide rational dose rates and schedules for clinical trials. A better understanding of the clinical pharmacology of these agents has suggested strategies to minimize their toxicity while maintaining therapeutic activity. (77 Refs.)
Tags: Animal; Human
Descriptors: *Cytarabine--therapeutic use--TU; *Fluorouracil--therapeutic use--TU; *Methotrexate--therapeutic use--TU; Drug Interactions; Drug Resistance; Fluorouracil--pharmacokinetics--PK; Fluorouracil--pharmacology --PD; Methotrexate--pharmacology--PD; Neoplasms--drug therapy--DT
CAS Registry No.: 147-94-4 (Cytarabine); 51-21-8 (Fluorouracil); 59-05-2 (Methotrexate)
Record Date Created: 19930111

11/5/16 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126246475 CA: 126(19)246475u JOURNAL
Thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer
AUTHOR(S): Johnston, Patrick G.; Mick, Rosemarie; Recant, Wendy; Behan, Katherine A.; Dolan, M. Eileen; Ratain, Mark J.; Beckmann, Enrique; Weichselbaum, Ralph R.; Allegra, Carmen J.; Vokes, Everett E.
LOCATION: NCI-Navy Medical Oncology Branch, Division of Clinical Sciences , National Cancer Institute, Bethesda, MD, USA
JOURNAL: J. Natl. Cancer Inst. DATE: 1997 VOLUME: 89 NUMBER: 4
PAGES: 308-313 CODEN: JNCIEQ ISSN: 0027-8874 LANGUAGE: English
PUBLISHER: Oxford University Press
SECTION:
CA201006 Pharmacology
IDENTIFIERS: thymidylate synthase fluoruracil head neck cancer, chemotherapy thymidylate synthase fluororacil neck cancer
DESCRIPTORS:
Antitumor agents...
head; thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer
Head...
neoplasm, inhibitors; thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer
Drug resistance... Interferon .alpha.2b...
thymidylate synthase expression and response to neoadjuvant

chemotherapy in patients with advanced head and neck cancer
CAS REGISTRY NUMBERS:
51-21-8 58-05-9 59-05-2 9031-61-2 15663-27-1 72732-56-0 thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer

11/5/17 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121292162 CA: 121(25)292162j JOURNAL
The role of P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein in the expression of differential sensitivities to antitumor agents in human tumor xenografts
AUTHOR(S): Mattern, Juergen; Volm, Manfred
LOCATION: Deutsches Krebsforschungszentrum, Heidelberg, Germany, D-69120
JOURNAL: Oncol. Rep. DATE: 1994 VOLUME: 1 NUMBER: 5 PAGES: 927-32
CODEN: OCRPEW LANGUAGE: English
SECTION:
CA201006 Pharmacology
IDENTIFIERS: P glycoprotein neoplasm inhibitor sensitivity, glutathione transferase pi antitumor agent sensitivity, thymidylate synthase neoplasm inhibitor sensitivity, metallothionein neoplasm inhibitor sensitivity
DESCRIPTORS:
Drug resistance... Glycophosphoproteins,P-... Metallothioneins... Neoplasm inhibitors...
P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts
CAS REGISTRY NUMBERS:
50-18-0 50-76-0 51-21-8 57-22-7 148-82-3 9031-61-2 15663-27-1 23214-92-8 P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts
50812-37-8 .pi.; P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts

11/5/18 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01556212 2675725
Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction.
Horikoshi, T.; Danenberg, K.D.; Stadlbauer, T.H.W.; Volkenandt, M.; Shea, L.C.C.; Aigner, K.; Gustavsson, B.; Leichman, L.; Danenberg, P.V.; et al.
1303 N. Mission Rd., Los Angeles, CA 90033, USA
CANCER RES. vol. 52, no. 1, pp. 108-116 (1992.)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Biochemistry Abstracts Part 2: Nucleic Acids

A polymerase chain reaction (PCR)-based method was used to quantitate the expression levels of low abundance genes relevant to cancer %drug% activity. RNA from %tumor% samples as small as 20 mg was isolated and converted to cDNA using random hexamers. We measured the relative %expressions% of %thymidylate% synthase, dihydrofolate reductase, and DT-diaphorase in a number of clinical %tumor% samples. Those tumors with the lowest %thymidylate% synthase %expression% had the best response to both the 5-fluorouracil-leucovorin and 5-fluorouracil-cisplatin combinations.

DESCRIPTORS: thymidylate synthase; dihydrofolate reductase; DT-diaphorase
IDENTIFIERS: genes; gene expression; levels; determination; polymerase chain reaction; tumours; man
SECTION HEADING: 14550 --General

11/5/19 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

13859025 PASCAL No.: 99-0036609
High basal level gene expression of thymidine phosphorylase (platelet-derived endothelial cell growth factor) in colorectal tumors is associated with nonresponse to 5-fluorouracil
METZGER R; DANENBERG K; LEICHMAN C G; SALONGA D; SCHWARTZ E L; WADLER S; LENZ H J; GROSHEN S; LEICHMAN L; DANENBERG P V
USC/Norris Cancer Center, University of Southern California School of Medicine, Los Angeles. California 90033, United States; Albert Einstein Cancer Center, Bronx, New York 10467, United States
Journal: Clinical cancer research, 1998, 4 (10) 2371-2376
ISSN: 1078-0432 Availability: INIST-26073; 354000071337060110
No. of Refs.: 46 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English

English Descriptors: Fluorouracil; Calcium folinate; %Drug% combination; Gene %expression%; Thymidine phosphorylase; Malignant %tumor%; Colon; Rectum; Human; %Thymidylate% synthase; Chemotherapy; Treatment efficiency ; Fluoropyrimidine derivatives; Pyrimidine derivatives; Antineoplastic agent
Broad Descriptors: Pentosyltransferases; Glycosyltransferases; Transferases ; Enzyme; Methyltransferases; Digestive diseases; Intestinal disease; Colonic disease; Rectal disease; Pentosyltransferases; Glycosyltransferases; Transferases; Enzyme; Methyltransferases; Appareil digestif pathologie; Intestin pathologie; Colon pathologie; Rectum pathologie; Pentosyltransferases; Glycosyltransferases; Transferases; Enzima; Methyltransferases; Aparato digestivo patologia; Intestino patologia; Colon patologia; Recto patologia

French Descriptors: Fluorouracil; Folinate de calcium; Association medicamenteuse; Expression genique; Thymidine phosphorylase; Tumeur maligne; Colon; Rectum; Homme; Thymidylate synthase; Chimiotherapie; Efficacite traitement; Fluoropyrimidine derive; Pyrimidine derive; Anticancereux; Leucovorine

Classification Codes: 002B02R02

11/5/20 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

13787522 PASCAL No.: 98-0501522
Mechanism and pharmacological specificity of dUTPase-mediated protection from DNA damage and cytotoxicity in human tumor cells
PARSELS L A; PARSELS J D; WAGNER L M; LONEY T L; RADANY E H; MAYBAUM J
Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109-0504, United States; Department of Radiation Oncology, University of Michigan Medical School, Ann Arbor, MI 48109-0504, United States
Journal: Cancer chemotherapy and pharmacology, 1998, 42 (5) 357-362

ISSN: 0344-5704 CODEN: CCPHDZ Availability: INIST-16820; 354000070976530020
No. of Refs.: 22 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Germany
Language: English
Purpose: We have reported previously that the expression of E. coli dUTPase (dutE) can protect HT29 cells from 5-fluorodeoxyuridine (FdUrd)-induced DNA fragmentation and cytotoxicity. In the study reported here. we further characterized the ability of dutE expression in one HT29 clone, dutE7. to alter the effects of treatment with FdUrd and other thymidylate synthase (TS) inhibitors. In addition, we developed two HuTu80 dutE-expressing clones using a pLNCX-dutE retroviral construct and tested their sensitivity to FdUrd-induced DNA fragmentation and cytotoxicity. Methods: Both a dutE retroviral expression system and a dutE antibody were developed to facilitate the generation and screening of dutE-expressing clones. HT29 and HuTu80 clones expressing dutE were tested for drug-induced DNA damage with either alkaline elution or pulsed field gel electrophoresis and drug-induced loss of clonogenicity. Results: Following a 24-h treatment with 100 mu M CB3717 or 500 n M methotrexate (MTX), dutE7 cells were significantly less sensitive to drug-induced loss of clonogenicity than con3 cells. DutE7 cells were also resistant to CB3717-induced DNA fragmentation at 24 h. However, following a 48-h treatment with CB3717 or MTX there was no difference in survival between con3 and dutE7 cells. even though DNA damage was still greatly attenuated in the dutE7 cell line. In addition, expression of dutE in two HuTu80 clones, 80 C and 80 K, did not protect these cells from FdUrd-induced DNA damage or cytotoxicity. Conclusions: We conclude that the role of uracil misincorporation and subsequent DNA damage in cytotoxicity induced by TS inhibitors, in HT29 cells, is time dependent, and that cytotoxicity caused by long-term exposure to these drugs is largely independent of resultant DNA damage, in this cell line. The inability of dutE to protect HuTu80 cells from FdUrd further suggests that the significance of uracil misincorporation resulting from TS inhibition varies among cell lines.
English Descriptors: Mechanism of action; Biological activity; Fluorouracil ; Cytotoxicity; Human; Malignant %tumor%; Colon; Established cell line; %Tumor% cell; In vitro; Antineoplastic agent; Chemotherapy; Uracil; Negative %therapeutic% reaction; Gene product; Fluoropyrimidine derivatives; Gene %expression%; dUTP pyrophosphatase; %Thymidylate% synthase
Broad Descriptors: Digestive diseases; Intestinal disease; Colonic disease; Hydrolases; Enzyme; Methyltransferases; Transferases; Appareil digestif pathologie; Intestin pathologie; Colon pathologie; Hydrolases; Enzyme; Methyltransferases; Transferases; Aparato digestivo patologia; Intestino patologia; Colon patologia; Hydrolases; Enzima; Methyltransferases; Transferases

French Descriptors: Mecanisme action; Activite biologique; Fluorouracil; Cytotoxicite; Homme; Tumeur maligne; Colon; Lignee cellulaire etablie; Cellule tumorale; In vitro; Anticancereux; Chimiotherapie; Uracile; Resistance traitement; Produit gene; Fluoropyrimidine derive; Expression genique; dUTP pyrophosphatase; Thymidylate synthase; Lignee HT29

Classification Codes: 002B04H03

11/5/21 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

13668018 PASCAL No.: 98-0376021
Thymidine phosphorylase moderates thymidine-dependent rescue after exposure to the thymidylate synthase inhibitor ZD1694 (Tomudex) in vitro

PATTERSON A V; TALBOT D C; STRATFORD I J; HARRIS A L
Experimental Oncology Group, Department of Pharmacy, University of Manchester, Manchester M13 9PL, United Kingdom; Imperial Cancer Research Fund, Clinical Oncology Unit, Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom
Journal: Cancer research : (Baltimore), 1998, 58 (13) 2737-2740
ISSN: 0008-5472 CODEN: CNREA8 Availability: INIST-5088; 354000077102220110
No. of Refs.: 18 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English
The inhibition of de novo thymidine (dThd) synthesis by the novel folate-based thymidylate synthase (TS) inhibitor ZD1694 (Tomudex) can achieve tumor cell-specific cytotoxicity in vivo. However, nucleosides in the surrounding microenvironment of tumors may be used by the salvage pathway to regenerate any depleted pools, thus providing an efficient mechanism through which to circumvent the ZD1694-dependent toxicity. Anabolism of dThd to dTMP by dThd kinase (TK) is the first committed step in the dThd salvage pathway. However, dThd phosphorylase (dThdPase) can compete with TK by catalyzing the reversible phosphorolytic cleavage of dThd to thymine and deoxyribose 1-phosphate and rendering the salvaged dThd metabolically unavailable. Both TK and dThdPase are up-regulated in some tumors, and their relative importance is not fully defined. We have studied the influence of dThdPase expression on the capacity of exogenous dThd to reverse ZD1694-dependent growth inhibition and have shown that both intra- and extracellular dThdPase activity can effectively moderate dThd-rescue. This suggests that tumor levels of dThdPase may be an important factor in the outcome of ZD1694 therapy.

English Descriptors: Enzyme inhibitor; Enzymatic activity; Cytotoxicity; Cytostase; Gene %expression%; Adenocarcinoma; Mammary gland; Gene product ; In vitro; Established cell line; %Tumor% cell; Negative %therapeutic% reaction; Human; Female; %Thymidylate% synthase; Thymidine kinase; Thymidine phosphorylase
Broad Descriptors: Methyltransferases; Transferases; Enzyme; Malignant tumor; Mammary gland diseases; Pentosyltransferases; Glycosyltransferases ; Methyltransferases; Transferases; Enzyme; Tumeur maligne; Glande mammaire pathologie; Pentosyltransferases; Glycosyltransferases; Methyltransferases; Transferases; Enzima; Tumor maligno; Glandula mamaria patologia; Pentosyltransferases; Glycosyltransferases

French Descriptors: Inhibiteur enzyme; Activite enzymatique; Cytotoxicite; Cytostase; Expression genique; Adenocarcinome; Glande mammaire; Produit gene; In vitro; Lignee cellulaire etablie; Cellule tumorale; Resistance traitement; Homme; Femelle; Thymidylate synthase; Thymidine kinase; Thymidine phosphorylase; Tomudex; ZD 1694; Lignee MCF7

Classification Codes: 002B02R02

11/5/22 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

13667477 PASCAL No.: 98-0375454
Variable expression of RFC1 in human leukemia cell lines resistant to antifolates
KOBAYASHI H; TAKEMURA Y; OHNUMA T
Department of Laboratory Medicine, National Defense Medical College, 3-2, Namiki, Tokorozawa, Saitama 359, Japan; Division of Neoplastic Diseases, Samuel Bronfman Department of Medicine, Mount Sinai School of Medicine, One

Gustave L. Levy Place, New York, NY 10029, United States
Journal: Cancer letters, 1998, 124 (2) 135-142
ISSN: 0304-3835 CODEN: CALEDQ Availability: INIST-17217; 354000076858530030
No. of Refs.: 33 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Ireland
Language: English

The resistance to folate-based antifolates is associated with impaired function of the reduced folate carrier (RFC), one of the major routes of folate transport into cancer cells. To clarify the importance of RFC functions in the antifolate resistance, we have examined the expression of RFCI and its phenotype as a folate transporter in human leukemia cell lines resistant to various antifolates. MOLT-3 cells resistant to ZD9331 (a thymidylate synthase (TS) inhibitor that utilizes the RFC for cell entry) (MOLT-3/ZD9331) showed decreased expression of RFCI concomitant with diminished cellular uptake of (SUP 3 H)methotrexate (MTX). K562 cells resistant to raltitrexed (ZD1694, another TS inhibitor that utilizes the RFC for cell entry) (K562/ ZD1694.C) scarcely expressed RFCI, which is in accordance with the impaired uptake of folate analogs and the high degree of resistance to ZD1694 and MTX. On the other hand, no apparent decrease of RFCI expression was found in transport-deficient MTX-resistant MOLT-3 cells (MOLT-3/MTX SUB 1 SUB 0 SUB 0 SUB 0 SUB 0) though its phenotype showed defective transport of MTX or ZD1694. In these cell lines with impaired RFC function, (SUP 3 H)leucovorin (LV) uptake was only moderately decreased as compared to (SUP 3 H)MTX or (SUP 3 H)ZD1694 uptake. These cells grew with a minimal retardation in folate-free medium supplemented with 10 nM LV, suggesting that these cell lines with impaired RFC function had enough folate transporters to transport LV. In contrast to downregulation of RFC, the much greater uptake of (SUP 3 H)MTX was observed in the MOLT-3/ trimetrexate (TMQ) SUB 8 SUB 0 SUB 0 -MTX SUB 1 SUB 0 SUB 0 SUB 0 SUB 0 in parallel with increased RFCI expression. These cell lines with the altered expression of RFCI may serve as models useful for investigating the regulation of RFCI expression and for understanding the molecular mechanism(s) behind the transport-mediated antifolate resistance.

English Descriptors: Calcium folinate; Trimetrexate; Methotrexate; Leukemia ; Human; Established cell line; %Tumor% cell; In vitro; Negative %therapeutic% reaction; Intracellular transport; Gene product; Antifolate ; Gene %expression%; Antineoplastic agent; Chemotherapy; %Thymidylate% synthase

Broad Descriptors: Malignant hemopathy; Methyltransferases; Transferases; Enzyme; Hemopathie maligne; Methyltransferases; Transferases; Enzyme; Hemopatia maligna; Methyltransferases; Transferases; Enzima

French Descriptors: Folinate de calcium; Trimetrexate; Methotrexate; Leucemie; Homme; Lignee cellulaire etablie; Cellule tumorale; In vitro; Resistance traitement; Transport intracellulaire; Produit gene; Antifolate; Expression genique; Anticancereux; Chimiotherapie; Thymidylate synthase; Gene RFC1

Classification Codes: 002B19B

11/5/23 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

13610261 PASCAL No.: 98-0315637
Molecular characterization of human acute leukemia cell line resistant to ZD9331, a non-polyglutamatable thymidylate synthase inhibitor
KOBAYASHI H; TAKEMURA Y; MIYACHI H
Department of Laboratory Medicine, National Defense Medical College, 3-2,

Namiki, Tokorozawa, Saitama 359-0042, Japan; Department of Clinical Pathology, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa 259-1193, Japan

Journal: Cancer chemotherapy and pharmacology, 1998, 42 (2) 105-110
ISSN: 0344-5704 CODEN: CCPHDZ Availability: INIST-16820; 354000076427060030
No. of Refs.: 24 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Germany
Language: English

ZD9331 is a non-polyglutamatable, potent quinazoline antifolate inhibitor of thymidylate synthase (TS). In an effort to clarify the exact mechanism of resistance to this novel TS inhibitor, we examined the molecular alterations in its target enzyme TS, the transport protein (reduced folate carrier, RFC), and folylpolyglutamate synthetase (FPGS) in a human acute lymphoblastic leukemia cell line, MOLT-3, made resistant to ZD9331. A 310-fold resistant sublime was established after 6 months exposure to the drug at concentrations up to 7 mu M, and was designated MOLT-3/ ZD9331. MOLT-3/ZD9331 showed crossresistance to CB3717 (4.8-fold), raltitrexed (63-fold) and methotrexate (MTX) (120-fold), but retained sensitivity to trimetrexate (0.88-fold). The resistant cells demonstrated impaired initial cellular uptake and low accumulation of (SUP 3 H)MTX in accordance with a decreased expression of RFC1, suggesting the downregulation of RFC. However, Southern blot analysis demonstrated no change in gene copy number nor gross rearrangement of RFC1 in the resistant cells. In addition, MOLT-3/ZD9331 showed amplification of the TS gene with a concomitantly increased level in the gene expression. In contrast, the expression of FPGS did not alter. These results

English Descriptors: Enzyme inhibitor; Methotrexate; Cross resistance; Chemotherapy; Human; Acute lymphocytic leukemia; Established cell line; %Tumor% cell; In vitro; Negative %therapeutic% reaction; Antineoplastic agent; Treatment; Gene %expression%; Gene product; Acute; %Thymidylate% synthase
Broad Descriptors: Malignant hemopathy; Lymphoproliferative syndrome; Methyltransferases; Transferases; Enzyme; Hemopathie maligne; Lymphoproliferatif syndrome; Methyltransferases; Transferases; Enzyme; Hemopatia maligna; Linfoproliferativo sindrome; Methyltransferases; Transferases; Enzima

French Descriptors: Inhibiteur enzyme; Methotrexate; Resistance croisee; Chimiotherapie; Homme; Leucemie lymphoblastique; Lignee cellulaire etablie; Cellule tumorale; In vitro; Resistance traitement; Anticancereux ; Traitement; Expression genique; Produit gene; Aigu; Thymidylate synthase; ZD 9331; Raltixered; Lignee MOLT3; CB 3717

Classification Codes: 002B02R02

11/5/24 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

13576213 PASCAL No.: 98-0278803
p53 point mutations and thymidylate synthase messenger RNA levels in disseminated colorectal cancer : An analysis of response and survival

LENZ H J; HAYASHI K; SALONGA D; DANENBERG K D; DANENBERG P V; METZGER R; BANERJEE D; BERTINO J R; GROSHEN S; LEICHMAN L P; LEICHMAN C G
University of Southern California/Norris Comprehensive Cancer Center, University of Southern California School of Medicine, Los Angeles, California 90033, United States; Memorial Sloan-Kettering Cancer Center, New York, New York 10021, United States

Journal: Clinical cancer research, 1998, 4 (5) 1243-1250
ISSN: 1078-0432 Availability: INIST-26073; 354000075848580200
No. of Refs.: 41 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English

English Descriptors: Malignant %tumor%; Colon; Rectum; Disseminated; Point mutation; TP53 Gene; %Thymidylate% synthase; Messenger RNA; Gene %expression%; Fluorouracil; Antineoplastic agent; Negative %therapeutic% reaction; Treatment; Chemotherapy; Treatment efficiency; Survival; Human; Fluoropyrimidine derivatives
Broad Descriptors: Methyltransferases; Transferases; Enzyme; Digestive diseases; Intestinal disease; Colonic disease; Rectal disease; Genetics; Methyltransferases; Transferases; Enzyme; Appareil digestif pathologie; Intestin pathologie; Colon pathologie; Rectum pathologie; Genetique; Methyltransferases; Transferases; Enzima; Aparato digestivo patologia; Intestino patologia; Colon patologia; Recto patologia; Genetica

French Descriptors: Tumeur maligne; Colon; Rectum; Dissemine; Mutation ponctuelle; Gene TP53; Thymidylate synthase; RNA messager; Expression genique; Fluorouracil; Anticancereux; Resistance traitement; Traitement; Chimiotherapie; Efficacite traitement; Survie; Homme; Fluoropyrimidine derive

Classification Codes: 002B13B01

11/5/25 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal

10001530 PASCAL No.: 92-0223816
Quantitation of thymidylate synthase, dihydrofolate reductase, ant DT-diaphorase gene expression in human tumors using the polymerase chain reaction
HORIKOSHI T; DANENBERG K D; STADBAUER T H W; VOLKENANDT M; SHEA L C C; AIGNER K; GUSTAVSSON B; LEICHMAN L; FROSING R; RAY M; GIBSON N W; SPEARS C P; DANENBERG P V
Univ. southern California school medicine, Kenneth Norris Jr cancer hosp., res. inst., Los Angeles CA 90033, USA
Journal: Cancer research : (Baltimore), 1992, 52 (1) 108-116
ISSN: 0008-5472 CODEN: CNREA8 Availability: INIST-5088; 354000023207790180
No. of Refs.: 24 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English Summary Language: English
A polymerase chain reaction (PCR)-based method was used to quantitate the expression levels of low abundance genes relevant to cancer drug activity. RNA from tumor samples as small as 20 mg was isolated and converted to cDNA using random hexamers. The 5' primers for the PCR contained a T7 polymerase promoter sequence, allowing the PCR-amplified DNA to be transcribed to RNA fragments. In each sample, the linear ranges of amplifcation of each cDNA of interest were established

English Descriptors: Malignant %tumor%; Human; Exploration; %Thymidylate% synthase; Tetrahydrofolate dehydrogenase; NADPH dehydrogenase (quinone); Gene %expression%; Quantitative analysis; Polymerase chain reaction; Complementary DNA; Chemotherapy; %Drug% combination; Treatment; Antineoplastic agent
Broad Descriptors: Enzyme; Enzyme; Enzima

French Descriptors: Tumeur maligne; Homme; Exploration; Thymidylate synthase; Tetrahydrofolate dehydrogenase; NADPH dehydrogenase (quinone); Expression genique; Analyse quantitative; Reaction chaine polymerase; DNA complementaire; Chimiotherapie; Fluorouracil; Association medicamenteuse; Leucovorine; Traitement; Anticancereux

Classification Codes: 002B04C

11/5/26 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

08434825 PASCAL No.: 88-0435713
Biochemical and molecular properties of cisplatin-resistant A2780 cells grown in folinic acid
YING LU; JUI HAN; SCANLON K J
City of Hope national medical cent., dep. medical oncology, Duarte CA 91010, USA
Journal: Journal of biological Chemistry, 1988, 263 (10) 4891-4894
ISSN: 0021-9258 CODEN: JBCHA3 Availability: CNRS-3082
No. of Refs.: 29 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: ENGLISH

English Descriptors: Folic acid; Cell culture; %Tumor%; Ovary; Human; Folic acid; Resistance; %Drug%; Transportation system; Aminoacid; Enzyme; Tetrahydrofolate dehydrogenase; Messenger RNA; Northern blotting; %Thymidylate% synthase; Gene %expression%; Metabolism

French Descriptors: Folique acide; Culture cellulaire; Tumeur; Ovaire; Homme; Folique acide; Resistance; Medicament; Systeme transport; Aminoacide; Enzyme; Tetrahydrofolate dehydrogenase; RNA messager; Methode Northern; Thymidylate synthase; Expression genique; Metabolisme; Lignee A2780; Cisplatine; DTMP synthase

Classification Codes: 002A04H01

11/5/27 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus

02538453 JICST ACCESSION NUMBER: 95A0629430 FILE SEGMENT: JICST-E
Applications of the Most Updated Biomedical Technology to Pathophysiology and Laboratory Medicine. Rapid Diagnosis of Drug-Resistant Genes by PCR Assay.
FUNATO TADAO (1)
(1) Tohoku Univ., Sch. of Med.
Rinsho Byori(Japanese Journal of Clinical Pathology), 1995, VOL.43,NO.6, PAGE.535-539, FIG.2, TBL.3, REF.10
JOURNAL NUMBER: Z0687AAS ISSN NO: 0047-1860 CODEN: RBYOA
UNIVERSAL DECIMAL CLASSIFICATION: 616-006-09 616-09
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Review article
MEDIA TYPE: Printed Publication
ABSTRACT: This report concerns the utility of the reverse transcription-polymerase chain reaction(RT-PCR) and quantitative PCR(QPCR) assay to detect the %drug%-resistance of related genes. The expression of some %drug%-resistance genes was compared with the

sensitivity and resistance-acquired %cancer% cell lines to anti-%cancer% drugs by Northern blot analysis and PCR assay. The resistance cell lines exhibited an enhanced %expression% of multi-%drug% resistance(MDR-1), %thymidylate% synthase(TS), c-fos and DNA polymerase .BETA. genes. Then these genes that %expressed% mRNA were quantitated using RT-PCR. The expression of the genes was dependent on their sensitivity (IC50) to anti-%cancer% drugs. Additionally, the QPCR assay has been developed as a rapid method for the expression of %drug% -resistance genes and applied to the PCR products amplified by the RT-PCR. Thus the QPCR assay for the expression of genes will allow rapid detection of the drug-resistance to chemotherapy in human cancers. (author abst.)

DESCRIPTORS: drug resistance; polymerase chain reaction; gene diagnosis; gene expression; early diagnosis; multiple drug resistance; drug resistance factor; dichlorodiammine platinum; quantitative analysis; tumor cell; human(primates)

BROADER DESCRIPTORS: resistance(endure); genetic technique; technology; DNA diagnosis; diagnosis; molecular genetic phenomenon; genetic phenomenon; phenomenon; factor; plasmid; ammine complex; complex(compound); coordination compound; compound(chemical); nitrogen compound; nitrogen group element compound; chloro complex; chloride; chlorine compound; halogen compound; halide; halogeno complex; antitumor drug; drug; platinum complex; platinum compound; platinum group element compound; transition metal compound; platinum group element complex; transition metal complex; metal complex; analysis(separation); analysis; idioblast ; cell(cytology)

CLASSIFICATION CODE(S): GE02030N; GC02040S

? logoff

01jul01 10:38:51 User208652 Session D467.6
$20.97 1.461 DialUnits File34
$96.60 23 Type(s) in Format 5
$96.60 23 Types
$117.57 Estimated cost File34
$2.54 0.453 DialUnits File5
$4.95 3 Type(s) in Format 5
$4.95 3 Types
$7.49 Estimated cost File5
$5.24 1.638 DialUnits File155
$1.80 9 Type(s) in Format 5
$1.80 9 Types
$7.04 Estimated cost File155
$6.15 0.490 DialUnits File399
$23.40 9 Type(s) in Format 5
$23.40 9 Types
$29.55 Estimated cost File399
$7.96 0.937 DialUnits File73
$2.35 1 Type(s) in Format 5
$2.35 1 Types
$10.31 Estimated cost File73
$1.05 0.206 DialUnits File76
$5.25 3 Type(s) in Format 5
$5.25 3 Types
$6.30 Estimated cost File76
$1.18 0.338 DialUnits File144
$12.40 8 Type(s) in Format 5
$12.40 8 Types
$13.58 Estimated cost File144
$2.27 0.315 DialUnits File71
$2.27 Estimated cost File71
$0.59 0.132 DialUnits File50
$0.59 Estimated cost File50
$0.71 0.202 DialUnits File94
$1.25 1 Type(s) in Format 5
$1.25 1 Types

$1.96 Estimated cost File94
$0.33 0.054 DialUnits File185
$0.33 Estimated cost File185
$0.74 0.275 DialUnits File156